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Comparison study between bacteriological aetiology and outcome of VAT & VAP

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ABSTRACT

Mechanical ventilation (MV) is a life saving process but it carries risks of respiratory tract infection as ventilator associated tracheobronchitis (VAT) and ventilator associated pneumonia (VAP) leading to increase morbidity and duration of mechanical ventilation in intensive care unit (ICU). VAT is an intermediate stage between colonization and VAP.

Aim of the work: To compare between VAT and VAP as regards microbiological diagnosis and outcome of patients.

Subjects and methods: The current study includes twenty patients admitted to respiratory ICU with respiratory failure developed VAT and VAP after 48 h of MV and to evaluate their impact on patient's outcome.

Results: Klebsiella was the commonest organism in both groups and that duration of stay on MV was observed in VAT patients and most of VAT patients progressed to VAP.

Conclusion: From the study we concluded that VAT infection is as severe as VAP and it needs more attention to prevent its presence as, once present, it usually progress to VAP increasing mortality rate in ICU.
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Introduction

Mechanical ventilation is life saving process but it carries risks of VAT and VAP which are associated with increase morbidity, duration of MV and mortality in ICU. VAT is believed to be an intermediate stage between colonization of the lower respiratory tract and VAP. However VAT may be a separate entity that may contribute to increase length of ICU stay and duration of MV Both VAP & VAT are clinically characterized by presence of fever, mucopurulent bronchial secretions & leukocytosis. In contrast to VAP, VAT does not involve pulmonary parenchyma and as a result does not cause radiographic pulmonary infiltrates. Accurate diagnosis of VAT is challenging as many conditions commonly encountered in critically ill patients can mimic its signs & symptoms [1].

Aim of the work

To document practice of clinical & microbiological diagnosis of VAT & VAP and to evaluate the impact of VAT & VAP on patient's outcome.

Subjects and methods

The study included twenty patients admitted to respiratory I.C.U suffering from respiratory failure and mechanically ventilated.

Exclusion criteria

- Patients with ongoing nosocomial infection.
- Pregnant women.
- Patients with community acquired pneumonia.
- Patients with neutropenia <1000 WBC/mm^3.

All patients were subjected to:

- Full history taking, general and local chest examination.
- Lab investigations (ABG, CBC and Renal function tests).

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- Follow up for developing lower respiratory tract Infection by daily assessment of
- patients as regards:
  1. Tracheal secretions quantity and character (Volume of secretions was graded according to the following scale: Scanty <30 ml/day and profuse >100 ml/day).
  2. Temperature
  3. PaO_2/FIO_2 twice weekly
  4. Assessment of chest X-ray twice weekly
  5. Leukocytic count
- Microbiological assessment by quantitative culture of respiratory secretion by Mini-BAL maneuver to take samples from lower respiratory tract.

Mini-BAL sampling was done at the first day of mechanical ventilation and after 48 h of mechanical ventilation.

Patients with positive culture after 48 h were included in the study. Patients were divided into two groups; group I (VAT) group II (VAP).

VAT diagnosed according to the following criteria:

Patient has no clinical or radiological evidence of pneumonia and has two of the following signs and symptoms in absence of other obvious cause:

- Fever (temp > 38 °C or < 36 °C).
- Leucocytosis > 12.000/mm^3.
- Sputum production; increase amount and change of color to yellow, greenish or pus.
- Positive cultures obtained by mini-BAL catheter (We used <10^3 as cut off value of colony count for positive culture for diagnosis of VAT. For diagnosis of VAP we used the same criteria for diagnosis of VAT with the development of CXR shadow suggestive of pneumonia, which equal to CPIS score >6 and we used 10^3 as cut off value of colony count for diagnosis of VAP) [2].

Mini- BAL technique

Materials used

a. Nelaton catheter size (18-FG), its distal end was cut and used as outer protective catheter.
b. Infant rhyle catheter size (10-FG) was used as the inner catheter and sterile K-y gel was used to block the distal end of the outer catheter.
c. Sterile gloves and 3 syringes 20 ml each of normal saline and a specimen container.

Procedure

According to Abd ElFattah et al.,[3] the Nelaton catheter used as outer catheter, was gently advanced into the endotracheal tube until resistance is met, indicating that the catheter is wedged into the distal airway, then retracted 4–5 cm. The infant rhyle catheter is advanced in a telescopic manner through the outer catheter extruding the K-y gel plug.

- A 20 ml syringe was connected to the inner catheter to administer its content of normal sterile saline that was aspirated again using the same 20 ml syringe while maintaining the catheter position. Aspiration process repeated until an appropriate specimen is obtained.
- The sample was poured into specimen container carefully to avoid contamination and close the lid tightly. Both catheters were removed together from the airways.
- Good closed suctioning of patient's airway was done.
- The samples taken were subjected to bacterial culture and colony count.
- All identified microorganisms were reported with their antibiotic sensitivities.

Bacterial culture and colony count

1. A 0.01 ml sterile calibrated loop was placed into the respective specimen and then onto the center of three media plates (blood agar, chocolate agar, and macconkey agar).
   The media plates were then streaked using the pin wheel streak method and incubated at 35 °C.
   Stained films from bacterial growth were examined by microscopy for the type of bacteria, Gram reaction (Gram-positive or Gram-negative) and morphology of the bacteria (cocci, diplococcic, rods or coccobacilli).
2. Bacterial culture growth was quantitated according to the number of colonies observed per plate were counted as follows:
   <10 colonies per plate represented <10^3 cfu / ml.
   10–100 colonies per plate represented 10^3–10^4 cfu/ml.
   100–1000 colonies per plate represented 10^4–10^5 cfu/ml.
   1000 colonies per plate represented >10^5 cfu/ml.
   All identified microorganisms were reported with their antibiotic sensitivities.

Results

Clinical criteria were as follows

- Group I:10 VAT patients received systemic antibiotics (100%) had colored secretions, 60% were profuse in amount, 40% were scanty, the mean temp. was (37.87 ± 0.47) the mean leucocytic count was (14.18 ± 5.04) × 10^3/ml the mean PaO_2/FIO_2 was (166.75 ± 39.9) and no patient has CXR shadows suggesting VAP (0%).
- Group II:
  10 VAP patients received systemic antibiotics(100%) had colored secretions, 30% were profuse, 70% were scanty, the mean temp. was (37.9 ± 0.69) °C the mean leucocytic count was (13.91 ± 6.47) × 10^3/ml, PaO_2/FIO_2 ratio was (166.20 ± 38.21) and the presence of CXR shadows suggestive of VAP were in (100%) of patients.

No significant difference between group I and group II on admission as regards clinical criteria (in comparing; secretion amount ($p = 0.234$), temperature($p = 0.542$) and Leucocytic count ($p = 0.457$), and in comparing PaO_2/FIO_2 ($p = 0.65$) (see Table 1).

The microbiological distribution of the micro organisms at day 1(Tables 2–5) showed that the commonest bacteria isolated from group I was klebsiella (60%) and from group II was klebsiella (90%).

Clinical outcome after 7 days of MV

Group I (VAT) showed that secretions were still colored in all patients, the amount decreased in 6 patients (60%), 4 patients (40%) had profuse amount . and group II (VAP), secretions were also still colored in all patients (100%) their amount decreased in 4patients (40%), 6patients (60%) had profuse amounts (Tables 7 and 8) and there was no significant difference between group I and group II as regards secretion outcome ($p = 0.337$) (see Table 6).

As regards temperature, group I showed that 4 patients (40%) had normal temperature 6 patients (60%) had high temp. with mean temp (37.75 ± 0.77)and group II showed 5 patients (50%) had normal temp. and 5 patients (50%) had high temp. with mean temp. (37.8 ± 1.23) °C. There was no significant difference between

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Table 1
Clinical criteria of VAT patients (group I) and VAP patients (group II).

Secretions	Group I VAT		Group II VAP		P value
	No	%	No	%	
Color					100% are colored
Colored	10	100	10	100	No needs for comparison
Not colored	0	0			
Amount					0.234
Scanty	4	40	7	70	>0.05
Profuse	6	60	3	30	NS
Temp.	37–38.5				0.542
Mean	37.87 ± 0.4				>0.05
Normal < 38°c	4	40	5	50	NS
High > 38°c	6	60	5	50	
Leucocytic count					0.457
<12,000	3	30	5	50	>0.05
>12,000	7	70	5	50	NS
Poa2/ FIO_2	137–255 (166 ± 39.9)		91–217.5 (166.20 ± 38.21)		0.65 NS
CXR	0	0	10	10	

Table 2
Isolated bacteria from VAT patients and their colony count.

Colony count	VAT pts.	
	No	%
Klebsiella 10^3	6	60%
MSSA staph aureus >10^4	1	10%
MRSA $\geqslant 10^5$	1	10%
Pseudomonas >10^6	1	10%
E. coli $\geqslant 10^4$	1	10%

This table shows that the commonest bacteria isolated in VAT group were klebsiella (60%).

group I and group II as regards temperature outcome (p = 0.827) (Table 9).

As regards total leucocytic count group I showed 5 patients (50%) had normal leukocytic count and 5 patients (50%) had high leukocytic count with mean count (13.15 ± 8.38) × 10^3/ml . group II showed 4 patients (40%) normal leukocytic count and 6patients (60%) had high leucocytic count and mean leucocytic count (15.36 ± 7.99) × 10^3/ml .There was no significant difference between group I and group II as regards leukocytic count outcome (p = 0.722) (Table 10).

Regarding PaO_2 /FIO_2 ratio in group 1 was (150.77 ± 34.56) and in group II was (160.89 ± 69.29). There was no significant difference between group I and group II as regards PaO_2 /FIO_2 outcome (p = 0.65) (Table 11).

Table 4
The bacteria isolated from VAP patients and their colony count.

Colony count	VAP pts.	
	No	10%
Staph aureus		
<10^3	0	0
>10^4	0	0
10^3	0	0
10^5	0	0
MRSA		
$\geqslant 10^5$	0	0
10^3	0	0
10^4	1	10
Klebsiella		
<10^3	0	
$\geqslant 10^4$	0	
>10^5	3	30
>10^6	4	40
10^3	2	20
10^4	0	
10^5	0	
Acinetobacter		
>10^4	0	0
>10^5	0	0
10^3	0	0
10^4	0	0
Pseudomonas		
<10^3	0	0
>10^6	0	0
E. coli		
$\geqslant 10^3$	0	0
>10^6	1	10

Table 3
Distribution of the drug sensitivity for bacteria isolated in VAT patients.

Sensitivity	MSSA	Klebsiella	Acinetobacter	*Pseudomonas*	*E. coli*	MRSA
Aminoglycosides	1	3	1 In combination		In combination	0
Quinolones		0	0	In combination	In combination	0
B. lactam	1	4	1 In combination	In combination	In combination	0
Carbapenem	0	5	0	0	0	0
Tazobact/pip sulbactam/cefiperazone	0	0	1	0	0	0
Macrolides	0	2	0	In combination	0	0
Doxycyclines	1	1	1	0	0	0
Vancomycine	0	0	0	0	0	1

As regard drug sensitivity of the bacteria isolated from VAT patients were (MSSA) were sensitive to aminoglycosides, blactam, doxycycline, MRSA was sensitive to vancomycin.
Klebsiella was sensitive to carbapenemc, B. lactam, aminoglycosides, macrolides, doxcycline. Acinetobacter was sensitive to Sulbactam /Cefiperazon + tazobactam /piperacillin, aminoglycosides & B. lectan in combination.
Pseudomonas was sensitive to B. lactam, quinolones, macrolides. *E. coli* was sensitive to aminoglycosides, quinolones and B. lactam.

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Table 5
Distribution of the drug sensitivity for bacteria isolated from VAP patients.

Sensitivity	MRSA (1)	Klebsiella (9)	Acinet 0	Pseudomonas	*E. coli* (1)	MASA
Aminoglycosides	0	2 (22%)	0	0	0	0
Quinolones	0	1 (11%)	0	0	0	0
B. lactame	0	0	0	0	0	0
Carbapenem	1 (100%)	5 (55%)	0	0	0	0
Tazobactam/piperacillin	0	0	0	0	0	0
Macrolids	0	0	0	0	0	0
Doxycyclines	0	0	0	0	0	0
Targocid	0	0	0	0	0	0

As regard drug sensitivity of the bacteria isolated from VAP pts were 55% of Klebsiella was sensitive to carbapenem followed by aminoglycosides (44%) and (11%) was sensitive to quinolones. *E. coli* was resistant to all antibiotics.

Table 6
Distribution of systemic antibiotics administered to the study group.

	Group I 10 pts.		Group II 10 pts.	
	No	%	No	%
Amikacin	2	20	6	60
Ceftazidine	5	50	6	60
Meropenam	1	10	3	30
Vancomycin	1	10	2	20
Imipenem	3	30	5	50
Levofloxacin	5	50	3	30
Cipro	5	50	4	40
Piperacillin/Tazo	5	50	3	30
Ceftriaxone	3	30	3	30
Clindamycin	1	10	2	20
Cefepime	4	40	3	30
Azithromycin	4	40	1	10
Sulperazon	1	10	2	20
Doxycyclines	0	0	1	10

Table 7
Comparison between groups as regards color of secretion.

Color of secretion	Group I		Group II		P value
	No	%	No	%	
Colored	10	100	10	100	100% are colored
Not colored	0	0	0	0	No needs for comparison

Table 8
Comparison between groups as regards secretion amount.

Amount	Group I		Group II		P value
	No	%	No	%	
Scanty	6	60	4	40	0.337
Profuse	4	40	6	60	>0.05 NS

Scanty amount <30 ml Profuse amount >30 ml

Table 9
Comparison between groups as regards temperature.

Temp.	Group I		Group II		P value
	No	%	No	%	
Range	37–39		36–40		0.827
	37.75 ± 0.72		37.8 ± 1.23		>0.05
Normal	4	40	5	50	NS
High	6	60	5	50	

Seven VAT patients (70%) progressed to VAP and 3 patients (30%) didn't.

As regards total MV days, the average for group I was (19.80 ± 13.83) days and for group II was (16.30 ± 5.21) days. There was no significant difference between group I and group II as regards MV days (p = 0.241) (Table 12).

As regards total ICU stay days, for group 1 was (20 ± 4.9) days and for group II was (21.8 ± 13.2) days. There was no significant difference between group I and group II as regards ICU stay days (p = 0.910) (Table 12).

As regards mortality group 1, 6 patients (60%) died, while 4 patients (40%) discharged and in group II 7 patients (70%) died and 3(30%) patients discharged. There was no significant difference

Table 10
Comparison between groups as regards Leukocytic count.

Leukocytic count	Group I		Group II		P value
	No	%	No	%	
Range X10^3/ml	4.9–27		8.4–34		0.722
(Mean ± SD) X10^3/ml	13.15 ± 8.38		15.36 ± 7.99		>0.05 NS
Normal	5	50	4	40	
High	5	50	6	60	

Normal WBCs 4000–11.000 c/um^3

Table 11
Comparison between groups as regards PaO_2/FIO_2 ratio.

PaO_2/FIO_2 ratio	Group I	Group II	P value
Range	105–202	74.4–280	0.65
(Mean ± SD)	151.27 ± 33.77	160.89 ± 69.29	NS

Table 12
Comparison between groups as regards MV days & ICU stay.

Outcome	Group I		Group II		P value
	Range	(Mean ± SD)	Range	(Mean ± SD)	
MV days	4–49	19.80 ± 13. 8	7–30	16 ± 15.2	0.241 NS
ICU stay days	7–51	20.7 ± 14.9	7–54	21.8 ± 13.2	0.91 NS

Table 13
Comparison between both groups as regards mortality.

Outcome	Group I		Group II		P value
Died	6	60%	7	70%	0.662
Survived	4	40%	3	30%	>0.05 NS
Causes of death	Septic shock (2) ARDS (2) Cardiac arrest (1) Cerebral infarction (1)		Septic shock (1) ARDS (2) Cardic. arrest (2) Bilateral pneumothorax (1) Pulmonary embolism (1)		0.754 >0.05 NS

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between group I and group II as regards mortality (p = 0.662). Causes of death in group I were septic shock, ARDS (20% for each of them), cardiac arrest, cerebral infarction (10% for each of them). Group II: ARDS and cardiac arrest (20% for each of them) septic shock, bilateral pneumothorax and pulmonary embolism (10% for each) (Table 13).

Discussion

Bronchitis and pneumonia are the most common hospital acquired infections in ICUs[4]. Ventilator associated pneumonia (VAP), remains the intensive care unit (ICU) infection associated with the highest morbidity and mortality and ventilator associated tracheobronchitis (VAT) is considered an intermediate condition between bacterial colonization and VAP. VAT and VAP have similar clinical presentations and microbiological diagnostic criteria, except that VAP requires a new and persistent infiltrate on chest X-ray [5].

IN the present study there was no significant difference between group I and group II on admission as regards clinical criteria (in comparing; secretion amount (p = 0.234), temperature (p = 0.542) and Leucocytic count (p = 0.457), and in comparing PaO_2/FIO_2 (p = 0.65).

VAT & VAP are caused by a wide range of bacterial pathogens, due to leakage around the endotracheal tube cuff or at time of intubation [6].

In the present study, the clinical criteria for diagnosis of VAT are matching with Nseir et al. [7] who studied the effect of developing VAT on outcome of 55 patients without chronic respiratory failure and also with Nseir et al. [8], study about the effect of antimicrobial treatment for VAT patients. on their outcome where VAT was identified by using certain criteria including fever >38 °C, new or increase sputum production positive endotracheal aspirate culture $\geqslant 10^6$ cfu/ml and no radiological evidence of nosocomial pneumonia.

In addition, the clinical criteria of VAT in the current study agree with Craven et al. [9], who followed up 188 mixed ICU patients intubated for >48 h for getting VAT or VAP by at least 2 clinical criteria (fever, leucocytosis or purulent sputum) for diagnosis of VAT plus persistent infiltrates for diagnosis of VAP.

In the present study the microbiological distribution (Tables 2–5) showed that the commonest bacteria isolated from group I was klebsiella (60%) and from group II was klebsiella (90%).

The microbiological criteria of the present study matches with Papazian et al. [10] who assessed the diagnostic accuracy of bronchoscopic techniques (BAL, PSB), and non bronchoscopic techniques (BBS and mini BAL) in the diagnosis of VAP and used 10^3 cFu/ml as the threshold of positivity for cultures obtained with mini- BAL samples and also matches with Josph Maria et al. [11] who compared the quantitative culture with the microscopic. examination of intracellular organisms of mini BAL samples for diagnosis of VAP & used positive quantitative cultures of the samples obtained by mini-BAL >10^3 cfu/ml. in addition the current study matches with Herve et al. [12] study who compared sampling methods; blind tracheal aspirate, blind protected telescopic catheter (mini:BAL technique) and bronchoscopic protected catheter for the diagnosis of VAP and had shown that the best threshold for blind protected telescopic catheter (mini- BAL) was between (10^2 and 10^3 cfu/m).

As regards drug sensitivity in the current study; klebsiella was sensitive to cabapenam, Aminoglycosides Macrolides, Acintobacter was sensitive to sulbactam (Cefiperazonet/Tazobactan/piperacillin, aminoglycosides, and B. Lactam. Pseudomonas was sensitive to B. lactain., Quinolones, Macrolides. E. Coli was sensitive to Aminoglycosides, Quinolones & to B. lactan.

The current study agrees with Nseir et al. [8] and Nseir et al. [13] who reported that Gram negative organisms were the most frequent isolates from VAT patients but pseudomonas was the highest percentage in their studies while i The current work also matches with that done by Dallas et al. [1] who found that Gram-ve organisms were the commonest organisms, of VAT patints, in addition, the present study agree with study done by Martin Loeches et al. [14] who also reported that VAT was frequently caused by Gram-negative bacteria, Pseudomonas, Acinetobacter Staph aureus, and also infection was polymicrobial in some patients with VAT. Also Carvent et al. [9] was similar to our study who found that Gram negative bacteria were the most frequent organisms isolated.

The current work agrees with the work done by Dallas et al. [1], and revealed that Gram negative bacteria were the commonest (64%) in VAP patients. Pseudomonas aeruginosa was the commonest (12.2%) Gram positive organisms accounted for (27.8%) and infection was polymicrobial in (19.3%) of patients. As regards amount, color of secretion, leucocytic count there was no significant difference between both groups in day 1 & day 5. As regard M. ventilator days and ICU stay there was no significant difference between Group I & Group II. Also as regard mortality rate and cause of death there was no significant difference between both groups.

In the present study there was no significant difference between group I and group II as regards secretion outcome (p = 0.337), or between group I and group II as regards temperature outcome (p = 0.827) (Table 9), or between group I and group II as regards leukocytic count outcome (p = 0.722) (Table 10) and no significant difference between group I and group II as regards PaO_2/FIO_2 outcome (p = 0.65) (Table 11).

Seven VAT patients (70%) in the present study progressed to VAP and 3 patients (30%) didn't progress to VAP.

As regards total ICU stay days in the present study; for group 1 was (20 ± 4.9) days and for group II was (21.8 ± 13.2) days. There was no significant difference between group I and group II as regards ICU stay days outcome (p = 0.910) (Table 12).

Regarding mortality in the current study; group I: 6 patients (60%) died, while 4 patients (40%) discharged and in group II 7 patients (70%) died and 3(30%) patients discharged. There was no significant difference between group I and group II as regards mortality (p = 0.662). Causes of death in group I were septic shock, ARDS (20% for each of them), cardiac arrest, cerebral infarction (10% for each of them). Group II: ARDS and cardiac arrest (20% for each of them) septic shock, bilateral pneumothorax and pulmonary embolism (10% for each) (Table 13).

In accordance with our study, in a prospective observational Cohort study by Craven et al. [15] of medical and surgical ICU patients, VAT was associated with increase length of ICU stay, more mechanical ventilator days, higher mortality in medical than surgical ICU patients. Nseir et.al. also demonstrated that appropriate antibiotic treatment was independently associated with decrease risk of transition from VAT to VAP [16].

There is increasing interest in using intravenous ± aerosolized antibiotics delivered by improved neubulizers, placed in the ventilators circuit, to treat more virulent organism, drug resistant pathogens such as staph aureus, *p. aerugniosa* and klebsiella pneumonia, aerosolized antibiotics therapy can deliver higher doses of antibiotics to the lung parenchyma that is not absorbed systemically & therefore decreased risk of Clostridium difficile infection [17].

Conclusion

From this study we concluded that, VAT infection is as severe as VAP and it needs more attention to prevent its presence as, once

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present, it usually progress to VAP increasing mechanical ventilation days, ICU stay days and mortality rate in ICU.

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